

### **REMARKS**

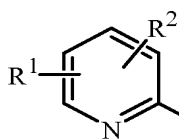
Claims 1-27 are pending in the application and stand rejected. Applicant respectfully requests reconsideration in view of the REMARKS herein.

Applicant thanks the Examiner for detailing the eligibility of the present application for continued examination in paragraph numbered 2 under the Detailed Action section. However, Applicant respectfully points out that no final action was issued by the Examiner in the present application. Applicant's request for continued examination under 37 CFR 1.114 was filed after receipt of a Notice of Allowance and was accompanied by submission of an Information Disclosure Statement.

### **Rejections under 35 U.S.C. 103(a)**

I. Claims 1-27 were rejected under 35 U.S.C. 103(a) as being unpatentable over Maurer et al. (DE1695659) and further in view of Bay et al. (*J. Org. Chem.* **1988**, 53, 2858-2859) and Fessenden (Fessenden et al., *Organic Chemistry* 4<sup>th</sup> Edition, Chapter 12 Substituted Benzenes, "Reactions of Benzenediazonium Salts", pp. 508-509). Applicant respectfully traverses this rejection. Applicant also respectfully requests that the Examiner make the publication date of Fessenden (4<sup>th</sup> Edition) of record.

Maurer et al. discloses a method for the preparation of 2-chloropyridines of the formula



wherein R<sup>1</sup> and R<sup>2</sup>, respectively, refer to a hydrogen atom or a halogen atom or an alkyl group with 1 to 4 carbon atoms – through conversion of a 2-aminopyridine, in which the reaction took place in a methanolic solution saturated with hydrogen chloride and with alkyl nitrites at a high temperature, characterized in that the mole ratio of 2-aminopyridine to methanol is 1:8 to 1:12 and the mole ratio of 2-aminopyridine to alkyl nitrite is 1:1 to 1:3.

First, Applicant directs the Examiner's attention to the fact that the disclosure in Maurer et al. is directed to the preparation of 2-chloropyridines from the corresponding 2-aminopyridines. There is no disclosure or examples directed to the preparation of 3-chloropyridines from 3-aminopyridines.

Second, Applicant respectfully points out that Maurer et al. provide a total of 15 examples, none of which disclose the use of a copper catalyst. Furthermore, there are no examples directed to the preparation of 3-chloropyridines from the corresponding 3-aminopyridines in the presence of a copper catalyst wherein at least about 50% of the copper is the copper(II) oxidation state. Specifically, Applicant directs the Examiner's attention to the fact that Maurer et al. state that 2-aminopyridines do not produce any isolatable diazonium salts and are only useful in coupling reactions under special conditions. Indeed absent from Maurer et al. is disclosure of the use of a copper catalyst wherein at least about 50% of the copper is the copper(II) oxidation state to facilitate "decomposition" of a diazo intermediate at any position of the pyridine.

A "decomposition" step is included in the present claims following diazotization of 2-chloro-3-aminopyridine and involves nucleophilic displacement on the pyridine diazonium intermediate by a chloride anion. Nucleophilic displacement reactions at the 2-position of a pyridine are generally known to proceed easily. In contrast, displacements at the 3-position of the pyridine are very difficult. Fessenden (Brooks/Cole Publishing 1998 6<sup>th</sup> ed. p. 806) describes this:

"It is not surprising, then, that nucleophilic substitution also occurs with pyridine. Substitution proceeds most readily at the 2-position, followed by the 4-position, but not at the 3-position. (Emphasis added)

Since Maurer et al. does not disclose the use of 3-aminopyridines, or the use of a copper catalyst or a copper catalyst wherein at least about 50% of the copper is the copper(II) oxidation state, and there is an expected difference in reactivity between the 2-position and 3-position of the pyridine, it is respectfully submitted that Maurer et al. do not suggest Applicant's Claims 1-27.

Applicant respectfully submits that combining Maurer et al. with Bay et al. and Fessenden (4<sup>th</sup> Edition) does not cure any of the deficiencies found in Maurer et al.

With respect to Fessenden (4<sup>th</sup> Edition), it is stated at pages 508-509 that an aryl amine can react with a nitrite to form an aryl diazonium salt, and when followed by the Sandmeyer reaction a copper(I) salt can be used as a source of a nucleophile to displace the N<sub>2</sub> on such aryl diazonium salts by halide ions (F<sup>-</sup>, Cl<sup>-</sup>, Br<sup>-</sup>, or I<sup>-</sup>) or a cyanide ion (-CN) to prepare aryl halides or aryl nitriles. The Cu<sup>+</sup> ion acts as a catalyst.

The explicit disclosure in Fessenden (4<sup>th</sup> Edition) is to *aryl* halides and not to *pyridyl* halides. There is no suggestion in Fessenden (4<sup>th</sup> Edition) that using copper(I) will work in ring systems other than phenyls and there is no mention of copper(II) at all.

Thus with respect to Fessenden (4<sup>th</sup> Edition) and its disclosure of the Sandmeyer reaction, Applicant respectfully maintains that it does not suggest the present invention due to the differences between phenyl and pyridine and the use of a copper(I) salt vs. a copper catalyst wherein at least about 50% of the copper is the copper(II) oxidation state.

With respect to Bay et al., this reference actually teaches the use of PTCP (phenyltetrachlorophosphorane) to convert 2-chloro-3-nitro-pyridine to 2,3-dichloropyridine in 81% yield in one step. Bay et al. actually “teaches away” from using the Sandmeyer reaction in favor of this new process being straightforward, inexpensive and high yielding.

Combining the teachings of Maurer et al., e.g. preparation of 2-chloropyridine from 2-aminopyridine, and further in view of Bay et al., e.g. conversion of a nitroaromatic to a chloroaromatic using PTCP, and Fessenden (4<sup>th</sup> Edition), e.g. preparation of aryl halides using copper(I) chloride, may not even suggest to one skilled in the art that contacting 2-nitropyridine with PTCP in methanol catalyzed by copper(I) chloride will produce 2-chloropyridine in higher yield (and at a lower cost). However, the combined teachings of Maurer et al. further in view of Bay et al. and Fessenden (4<sup>th</sup> Edition) most certainly do not suggest present Claims 1-27 and in fact teach away from using the Sandmeyer reaction including substituting therein a 3-aminopyridine or substituting therein a copper catalyst wherein at least about 50% of the copper is the copper(II) oxidation state.

II. Claims 1-27 were rejected under 35 U.S.C. 103(a) as being unpatentable over Bay et al., and further in view of Fessenden (4<sup>th</sup> Edition). Applicant respectfully traverses this rejection.

As discussed above, Bay et al. teach the use of PTCP (phenyltetrachloro-phosphorane) to convert 2-chloro-3-nitro-pyridine to 2,3-dichloropyridine in 81% yield in one step. Mention is made of the Sandmeyer reaction in Bay et al. as a prior solution to the substitution of aromatic nitro groups by chlorine. However, Bay et al. actually “teaches away” from using the Sandmeyer reaction in favor of their new process which is touted as being straightforward, inexpensive and high yielding.

In Bay et al. 3-nitro-2-chloropyridine is converted directly to 2,3-dichloropyridine using two readily available organophosphorus reagents. Table I of Bay et al. shows yields for the conversion of such nitroaromatics to chloroaromatics and their corresponding % yield. In the process of Bay et al. there is no reduction of a nitro group to an amine and no diazotization. In addition as can be noted from page 2859, no radical decomposition is demonstrated and their reaction scheme shows no such reduction, and thus the mechanism is completely different from that of the Sandmeyer reaction. Further, no mention is made of catalytic decomposition using either a copper(I) catalyst or a copper catalyst wherein at least about 50% of the copper is the copper(II) oxidation state.

Applicant's process uses a completely different starting material, i.e. 3-amino-2-chloropyridine, than that described by Bay et al. The Examiner stated that the starting material of Bay et al., 3-nitro-2-chloropyridyl, is reduced to the corresponding amine and that this step is neither disclosed or disclaimed in the present process. However, as discussed above, Applicant respectfully submits that there is no disclosure or suggestion in Bay et al. of their 3-nitro-2-chloropyridyl starting material being reduced to the corresponding amine.

Bay et al. discloses an alternative method to the Sandmeyer reaction. The new reagent PTCP (and not reduction, diazotization and nucleophilic displacement catalyzed by copper(I) as suggested by the Examiner) is disclosed as being useful for the regiospecific preparation of chloro aromatic compounds. The textbook teaching from Fessenden (4<sup>th</sup> Edition, page 508) proposes a mechanism for the nucleophilic displacement of benzenediazonium salts. As discussed above, these nucleophilic displacements are not expected to react in the same manner in pyridine rings, and furthermore, are not expected to react in the same manner at the 3- versus the 4-position of the pyridine ring.

Bay et al. and Fessenden (4<sup>th</sup> Edition) disclose two separate and distinct reactions which proceed by different mechanisms and utilize different starting materials. Therefore, Applicant respectfully maintains that the combined teachings of these two reactions are uncomplimentary and will result in an inoperable process.

Accordingly, Applicant respectfully submits that Claims 1-27 are not suggested by Bay et al. alone or further in view of Fessenden (4<sup>th</sup> Edition).

**Information Disclosure Statements**

I. Applicant brings to the Examiner's attention a Supplemental Information Disclosure Statement that is being filed concurrently with this RESPONSE.

II. Applicant thanks the Examiner for attaching a copy of Applicant's PTO/SB/08B form showing consideration of the references listed thereon. However, Applicant has noted that Cite No. 4, EMANUEL PFEIL ET AL., "On the Sandmeyer Reaction Pfeil et al. and Cite No. 7 H. ZOLLINGER have not been initialed by the Examiner. It is Applicant's understanding that a line drawn through a citation means that it is not in conformance and not considered.

Applicant respectfully requests that the Examiner explain why Cite Nos. 4 and 7 are deemed not in conformance and not considered. Applicant notes that both cites are available on PRIVATE PAIRS in their entirety as well as an English translation of the PFEIL citation.

In view of the foregoing, allowance of the above-referenced application is respectfully requested.

Respectfully submitted,

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Dated: October 1, 2009